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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/791,628	03/01/2004	Benjamin G. Davis	GC571-2-C1	3111

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Genencor International, Inc.
925 Page Mill Road
Palo Alto, CA 94034-1013

EXAMINER	
MEAH, MOHAMMAD Y	
ART UNIT	PAPER NUMBER
1652	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/791,628	DAVIS ET AL.	
	Examiner	Art Unit	
	MD. YOUNUS MEAH	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 April 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7,8,19-23,25,26,32-40,44-47,56-60,62,63,69,70,72 and 73* is/are pending in the application.

4a) Of the above claim(s) *37-40,44-47,56-60,62,63 and 69-73* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5, 7-8, 19-23, 25-26 and 32-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-5, 7-8, 19-23, 25-26, 32-40, 44-47, 56-60, 62-63, 69-70 and 72-73 are pending. With supplemental amendment of this application, the applicant, on 04/5/010 amended claims 1, 4, 33 and cancel claim 9. Claims 37-40, 44-47, 56-60, 62-63 and 69-73 remain withdrawn. Claims 1-5, 7-8, 19-23, 25-26 and 32-36 are for examination.

Applicants' response of 04/5/010 is acknowledged. Applicants' arguments filed on 04/5/010 have been fully considered but they are found unpersuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim objections

Claim 1 is objected to for reciting "A catalytic ---- target molecule". It should be "A catalytic antagonist of a target molecule, wherein said antagonist comprises a targeting moiety that specifically binds---- target molecule". Appropriate correction is required.

Claim Rejections35 U.S.C 112 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 2-5, 7-8 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3 and 4-5, 7-8 (depend on claim 3) remain indefinite because of the following reason: It is unclear whether cysteine of claim 2 is substituted by a native

amino acid other than cysteine, or the native amino acid in the enzyme is substituted with a cysteine." If the cysteine of claim 2 is substituted for a native amino acid other than cysteine, how is one going to have a targeting moiety joined to the enzyme through a sulfur group? It appears from the specification that the native amino acid in the enzyme is substituted with a cysteine so that the sulfur group would link the moiety to the enzyme. Correction is required

Claim 4 remains indefinite in the recitation of the phrase “amino acid position adjacent to the subsite" because the subsite is defined as a portion of the protein comprising a substrate binding site. Since this definition does not define an N-terminus or a C-terminus for the subsite, it is unclear as to what would be considered an amino acid position adjacent to the subsite. Also it is unclear what is a “van der Waals contact with the subsite” referring to.

Claim 5 remains indefinite in the recitation of the phrase “an amino acid forming a substrate binding site “because it is unclear what an amino acid forming a substrate binding site is.

Applicants’ arguments against the rejection of claims 3 and 4-5 are considered but found unpersuasive. Applicants argue that the language substituted for refers to substitution of any amino acid by a cysteine. However claim 2 refers to cysteine of the unmodified enzyme not the modified enzyme.

Applicants further argue that the term substrate binding site and Van der Waals are well defined terms. Applicants’ argument is considered but found unpersuasive. As explained above the subsite is defined as a portion of the protein comprising a substrate

binding site. Since this definition does not define an N-terminus or a C-terminus for the subsite, it is unclear as to what would be considered an amino acid position adjacent to the subsite. Also it is unclear what is a "van der Waals contact with the subsite" referring to.

Claim Rejection - 35 U.S.C 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-5, 7-8, 19-23, 25-26, 32-34 and 36 remain rejected under 35 U.S.C. 102(a) as being anticipated by Davis, et al. (J. org. chem. 19998, pp 9614-9615) for reasons of record.

Davis et al. teach *B. subtilisin* proteases conjugated to carbohydrates such as mannose wherein cysteine residue is introduced to S1 subsite by a substitution (page 9614, column 2, 2nd paragraph) at a preselected position enabling the highly reactive thiol group to react with an activated carbohydrate moiety (page 9614, column 2 paragraph 1). The enzyme conjugate comprising said protease conjugated to a carbohydrate comprises binding ability to a lectin, like conA and the ability to cleave the lectin molecule by the said protease domain. It is well known in the art that a carbohydrate bind lectins, such as concanavalin A (conA), selectin and other cell surface carbohydrate binding proteins, including blood (blood comprise selectins) stain

(soil) (see Wang et al. JBC 1975, 250, 1490-1502). ConA and other lectins are involved in the interaction of cell surface receptors and other ligands comprising glycoproteins (Wang et al. page 1490). It is well known in the art that subtilisins are broad specificity serine proteases and would be expected to cleave a peptide bond in a target protein such as lectins or selectins (see Wang et al page 1491, column 1, subtilisin protease cleave conA).

Arguments and response

Applicants arguments at pages 9-10 in their amendment of 4/5/10 traversing the USC 102(a) rejection of claims 1-5, 7-8, 19-23, 25-26, 32-34 and 36 have been fully considered, but they are not found persuasive.

Applicants argue that the invention of claim 1 is a catalytic antagonist of a target molecule, comprising a carbohydrate targeting moiety that specifically binds to the target molecule attached to a subtilisin-type serine protease, wherein the protease degrades the target molecule to reduce its binding to targeting moiety, resulting in the release of the antagonist, allowing it to bind and degrade another target molecule. Applicant further argue that Davis et al. do not teach a particular carbohydrate moiety for binding to a target molecule, that the glycosylated polypeptide would bind to a target molecule, that the glycosylated polypeptide would degrade a target molecule, or that the glycosylated polypeptides would be regenerated and made available to degrade an additional target molecule. None of these features necessarily follow from what is described in Davis et al.; therefore, the reference does not inherently anticipate the present claims. Applicants' arguments have been fully considered, but they found

unpersuasive, Davis et al. teach *B. subtilisin* protease conjugated to carbohydrates such as mannose and said conjugate is inherently a catalytic antagonist of a target molecule, comprising a carbohydrate targeting moiety that specifically binds to the target molecule attached to a subtilisin-type serine protease, wherein the protease degrades the target molecule to reduce its binding to targeting moiety.

Claim Rejection - 35 U.S.C 103a

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a)A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 35 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Davis et al. (J. org. chem. 19998, pp 9614-9615).), in view of Nilsson et al (Glycoconjugate 1998, 219-223) for reasons of record.

Davis et al. teach *B. subtilisin* protease conjugated to carbohydrates such as mannose wherein cysteine residue is introduced to S1 subsite by substitution (page 9614, column 2, 2nd paragraph) at a pre-selected position enabling the highly reactive thiol group to react with an activated carbohydrate moiety (page 9614, column 2 paragraph 1). However Davis et al. do not teach said mannoside as thioethyl mannoside.

Nilsson et al teach the use of thioethyl glycoside as a building block in carbohydrate synthesis. Nilsson et al teach also the advantage of thioglycoside, such

stable under most reaction conditions, can be activated easily (page 219 1st paragraph.) Therefore, one knowledgeable in prior art is motivated to make a chimeric protein comprising B. subtilisin protease conjugated to mannose via thioethyl mannoside.

As such it would have been obvious to one of ordinary skill in the art to use thioethyl mannoside to conjugate B. subtilisin type protease as taught by Davis et al. Expectation of success is high at replacing any carbohydrate targeting moiety by a thioethyl mannoside because thioethyl mannoside is a carbohydrate and above prior arts teach that thioethyl mannoside is easy to make and it binds lectin such as conA.

Arguments and response

Applicants arguments at pages 10-11 of their amendment of 06/29/09 against the use of USC 103(a) rejections for claims 35 have been fully considered, but they are not found persuasive.

Applicants argue that neither Davis et al. nor Nilsson et al., separately or in combination, teach or suggest the features of claim 1, it is immaterial whether Nilsson et al. teach the additional limitation of claim 35. Applicants' arguments have been fully considered, but they found unpersuasive, As explained above, Davis et al. teach *B. subtilisin* protease conjugated to carbohydrates such as mannose and said fusion protein inherently is a catalytic antagonist of a target molecule, comprising a carbohydrate targeting moiety that specifically binds to the target molecule attached to a subtilisin-type serine protease, wherein the protease degrades the target molecule to

reduce its binding to targeting moiety, resulting in the release of the antagonist, allowing it to bind and degrade another target molecule. Furthermore; a thioethyl mannoside type carbohydrate targeting moiety is easy to make and it binds lectins such as conA.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mohammad Meah whose telephone number is 571-272-1261. The examiner can normally be reached on 8:30-5PM.
If attempts to reach the examiner by telephone are unsuccessful, the examiner's Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mohammad Younus Meah
Examiner, Art Unit 1652

/Delia M. Ramirez/
Primary Examiner, Art Unit 1652